

Improving the Sensitivity of Epidemiologic Studies

2004 Epidemiology, Biostatistics and Clinical
Research Methods Summer Session
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Part 19

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- Uncertain about how to distinguish the many false alarms [produced by epidemiologic research] from the few that may be true, the public and nonepidemiologic scientists are confronted by evidence that is peer-group approved but scientifically inadequate.

Feinstein AR, Science 1988;242:1267-63

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- In epidemiology, victories are few and at this point a whole field may be on the verge of propagating pathological science, which means they cannot get good enough resolution to identify the effects they're studying. Epidemiologists may be seeing and reporting that there are canals on Mars because they're looking at Mars through Galileo's telescope. And that's the nature of the field and all the statistical wizardry in the world isn't going to change that.

Taubes G, Epidemiology Monitor 1996;17:1-14

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- Weak associations, so far from being the Achilles heel of epidemiology that critics and representatives of vested interests would like to make out, are among its most important contributions; they may be socially of great importance and can often be revealed only by epidemiological investigation.

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- They are certainly difficult to establish and to interpret, but their establishment and correct interpretation is a challenge that modern epidemiologists should willingly accept.

Doll R, J Epidemiol 1996;6:S11-20

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One response to Doll's challenge:

- Are there ways of designing and analyzing epidemiologic studies to allow otherwise weak associations to become stronger?

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Strategies for Increasing the Sensitivity of Epidemiologic Studies to Identify a True Association Between Exposure and Disease

- I. Minimize errors of measurement
- II. Subclassify exposure status
- III. Allow for the existence of other causal pathways that give rise to the disease
 - A. Assess the determinants of a causal exposure itself
 - B. Analyze separately classes of diseased individuals that differ according to one or more features of their disease
 - C. Analyze separately subjects in whom another risk factor for the disease was or was not present

Am J Epidemiol 1983;117:14-18

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Source of drinking water in three subdistricts of South London, 1854

<u>Water company</u>	<u>Source</u>
Southwork & Vauxhall	Thames, near London (ocean salinity)
Lambeth	Upstream (less salinity)

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- The canard that godliness and goodliness are linked in any way but typographically must be taken on faith, for no evidence supports it. [For example,] recent data compiled on the religious views among federal prisoners show that nonbelievers account for less than 1% of the total, significantly lower than for America as a whole.

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Admittedly, some of those true-believing inmates may have converted post-incarceration.

Natalie Angier
"Confessions of a Lonely Atheist"
NY Times Magazine 1/14/01

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Observation in the early 1970s:

Among pre-menopausal women diagnosed with endometrial cancer who had previously taken OCs, an atypically high proportion had taken Oracon.

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Could this observation be explained by:

- a) A high risk of cancer among Oracon users?
- b) A low risk among users of other OCs?
- c) Both of the above?

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Use of combined oral contraceptives¹ among women with endometrial cancer and among controls

<u>Combined OC use</u>	<u>Cases</u>	<u>Controls</u>	<u>Relative risk²</u>	<u>95% confidence limits</u>
Yes	17	76	0.5	0.1 – 1.0
No	93	173	1.0	---

- 1. Subjects with sequential oral contraceptive use for one or more years are excluded.
- 2. Standardized for age and use of menopausal estrogens.

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Use of sequential oral contraceptives among women with endometrial cancer and among controls

<u>Sequential OC use</u>	<u>Cases</u>	<u>Controls</u>	<u>Relative risk¹</u>	<u>95% confidence limits</u>
Yes	7	19	2.2	0.6 – 7.3
Oracon	6	8	7.3	1.4 – 38.8
Other	1	11	0.3	0.0 – 2.9
No	110	376	1.0	---

- 1. Standardized for age, use of combined OCs, and use of menopausal estrogens.

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Am J Epidemiol 1983;117:14-18

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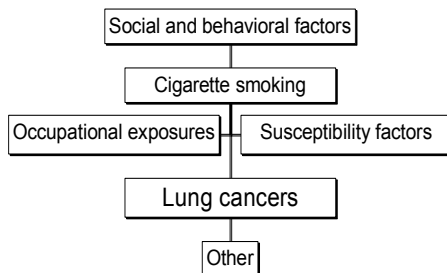
- Two possible studies of the role of social and psychological factors in adolescence on the risk of lung cancer

- 1) Case-control study of lung cancer
- 2) Case-control study of teenage smoking

- Which is more likely to contribute information relevant to the etiology of lung cancer?

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Causal Pathways to Lung Cancer



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Psychosocial Factors and Risk of Hypertension

- **Context**

Although psychosocial factors are correlated, previous studies on risk factors for hypertension have typically examined psychosocial factors individually and have yielded inconsistent findings.

JAMA. 2003;290:2138-2148 19

Psychosocial Factors and Risk of Hypertension

- **Objective**

To examine the role of psychosocial factors of time urgency/impatience (TUI), achievement striving/competitiveness (ASC), hostility, depression, and anxiety on long-term risk of hypertension.

JAMA. 2003;290:2138-2148 20

Psychosocial Factors and Risk of Hypertension

- **Design, Setting, and Study Population**

A population-based, prospective, observational study using participant data from the Coronary Artery Risk Development in Young Adults (CARDIA) study. A total of 3308 black and white adults aged 18 to 30 years (when recruited in 1985 and 1986) from 4 US metropolitan areas and followed up through 2000 to 2001.

JAMA. 2003;290:2138-2148 21

Psychosocial Factors and Risk of Hypertension

- **Main Outcome Measures**

Fifteen-year cumulative incidence of hypertension (systolic blood pressure of 140 mm Hg or higher, diastolic blood pressure of 90 mm Hg or higher, or taking antihypertensive medication).

JAMA. 2003;290:2138-2148 22

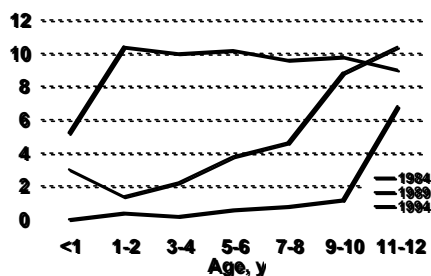
Psychosocial Factors and Risk of Hypertension

- **Conclusion**

Among young adults, TUI and hostility were associated with a dose-response increase in the long-term risk of hypertension.

JAMA. 2003;290:2138-2148 23

Age-specific Prevalence of Hepatitis B Surface Antigen (HBsAg) in Children in 1984, 1989 and 1994



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Incidence of liver cancer in 6-9 year-old children in relation to hepatitis B vaccination: Taiwan

Birth cohort	Population (in millions)	# of cases	Annual incidence per million
Pre-vaccination (7/74 – 6/84)	15.7	82	5.2
Post-vaccination (7/84 – 6/86)	2.3	3	1.3

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Serological evidence of *H. pylori* infection in persons with gastric carcinoma and controls

Location of tumor	n	% infected	Odds ratio
Stomach per se	109	84.4	3.6
Gastroesophageal junction	27	63.0	0.8

N Engl J Med 1991;325:1127-31

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Examples of Separate Classes of Diseased Individuals

- 1) Infectious diseases
 - Enteritis caused by salmonella infections of differing serotypes and plasmid content
- 2) Cancer
 - Histologic types of lung cancer
 - Cytogenetic types of leukemia
 - Presence of particular oncogene(s)?
- 3) Cardiovascular disease
 - Cerebral hemorrhage or thrombosis

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- In the first four weeks of the epidemic, the proportion of fatal attacks to each 10,000 houses was as follows: Southwark and Vauxhall, 71; Lambeth, 5. The cholera was therefore 14 times as fatal at this period among persons having the impure water of the Southwark and Vauxhall Company, as among those having the purer water.

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- As the epidemic advanced, the disproportion between the number of cases in houses supplied by the Southwark and Vauxhall Company and those supplied by the Lambeth Company became not quite so great. Cholera would necessarily spread amongst the customers of the Lambeth Company, as in parts of London where the water was not in fault, by all the usual means of its communication.

Snow J, On the Mode of Communication of Cholera, 1855

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Q. When we increase the number of comparisons as a means of increasing the sensitivity of our studies, don't we run the risk of decreasing their specificity? That is, won't we begin to observe more and more spurious associations?

A. Yes.

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• "We conducted a case-control study to determine whether a polymorphism in the CYP 17 gene was associated with risk of breast cancer. We found an increased risk of advanced breast cancer in women carrying an A₂ allele. The OR was 2.5 (95% CI = 1.07 – 5.94) for regional or metastatic disease. . . These findings suggest that the CYP 17 genotype may be a biomarker for advanced breast cancer risk."

Abstract of article in Cancer Res 1997;57:1063-65

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CYP Polymorphism and Breast Cancer – Results

	n	% with ≥ 1 A ₂ allele	OR	95% CI
Controls	285	66.3	--	--
Cases				
Localized	134	68.7	1.1	0.7 – 1.8
Advanced	40	82.5	2.5	1.1 – 5.9
Total	174	71.8	1.3	0.9 – 2.0

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- The interpretation of a difference in the presence or size of an association among subgroups should be made with considerable caution unless:
 - 1) That difference is large;
 - 2) It is based on a large number of subjects;
 - 3) There is a plausible explanation for the difference.

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Case-control Study of Testicular Cancer

History of vasectomy in cases and controls,
by religion

	% of cases	% of controls	Relative risk
Catholic	24.4	6.2	8.7
Other	23.0	19.6	1.2

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- III. C. Analyze separately subjects in whom another risk factor for the disease was or was not present

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